

## Developmental Pyrethroid Exposure Reproduces Features of Attention-Deficit Hyperactivity Disorder

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**Background:** Attention-deficit hyperactivity disorder (ADHD) is estimated to affect 3–12% of school-age individuals in the United States alone. Although the pathophysiology of ADHD is not completely understood, disruption of the dopaminergic system appears to play a central role. While genetic factors account for a large percentage of ADHD, an estimated 20–40% of cases do not appear to have a primary genetic etiology, suggesting that environmental factors may contribute to ADHD. Accordingly, exposure to environmental agents, such as pesticides, that alter the proper development of the dopaminergic system may contribute to ADHD.

**Methods:** C57 BL/6j mice were administered 0, 0.3, 1, or 3 mg/kg deltamethrin (DM) dissolved in corn oil and mixed with peanut butter every three days throughout gestation and lactation. Offspring were weaned on postnatal day 22, and experiments were conducted on mice 6–12 weeks of age.

**Results:** Gestational–lactational exposure to DM increased dopamine transporter (DAT) levels (21%, 35%, and 70%) in male offspring as determined by western blotting, which is in the same range of increased DAT levels observed in ADHD patients. These mice also exhibited marked hyperactivity (98%, 131%, and 185% increase in locomotor activity), which was reversed by therapeutically relevant doses of methylphenidate (0.1 mg/kg), and deficits in working memory and attention. Gene-profiling studies revealed a dose-related increase in the transcription factors Nurr1 (1.3–2-fold) and Pitx3 (1.4–2.2-fold), which are required for proper development of the dopamine system and regulation of DAT expression.

**Conclusions:** The parallels between mice developmentally exposed to deltamethrin and individuals with ADHD suggest that it may be prudent to evaluate pyrethroid exposure as a risk factor for ADHD.

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